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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/040,077
Filing Date	January 4, 2002
First Named Inventor	Terry Amiss
Art Unit	1743
Examiner Name	Alexander, L
Attorney Docket Number	0709.017.0002

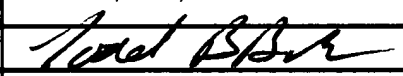
Total Number of Pages in This Submission: 7

ENCLOSURES *(Check all that apply)*

- [✓] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [✓] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [✓] Other Enclosure(s) (please Identify below):

Remarks: Enclosed is a courtesy copy of a Reply origianlly filed March 22, 2004 and resubmitted, via facsimile, May 26, 2004.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Todd B. Buck, Ph.D.; Reg. No. 48,574 Castellano, Malm, Ferrario & Buck
Signature	
Date	June 25, 2004

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Typed or printed name	Todd B. Buck		
Signature		Date	June 25, 2004

PTO/SB/17 (10-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 1330.00

Complete if Known	
Application Number	10/040,077
Filing Date	January 4, 2002
First Named Inventor	Terry Amiss et.al
Examiner Name	Alexader, L
Art Unit	1743
Attorney Docket No.	0709.017.0002

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 50-3120

Deposit Account Name:

The Director is authorized to: *(check all that apply)*

☐ Charge fee(s) indicated below ☐ Credit any overpayments

☐ Charge any additional fee(s) or any underpayment of fee(s)

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

		Extra Claims		Fee from below	Fee Paid
Total Claims	0	-20** = 0	X	18.00	= 0.00
Independent Claims	0	- 3** = 0	X	86.00	= 0.00
Multiple Dependent				0.00	= 0.00

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0.00

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	1,330.0
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($)

SUBMITTED BY				(Complete *(if applicable)*)	
Name (Print/Type)	Todd B. Buck	*Registration No. (Attorney/Agent)*	48,574	*Telephone*	202-478-5300
Signature				*Date*	June 25, 2004

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IFW Date 1/4

PTO/SB/64 (11-03)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNINTENTIONALLY UNDER 37 CFR 1.137(b)	Docket Number (Optional) 0709.017.0002

First named inventor: Terry Amiss

Application No.: 10/040,077 Art Unit: 1743

Filed: January 04, 2002 Examiner: Alexander, L

Title: Binding Protein as Biosensors

Attention: Office of Petitions
Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
FAX: (703) 872-9306

NOTE: If information or assistance is needed in completing this form, please contact Petitions Information at (703) 305-9282.

The above-identified application became abandoned for failure to file a timely and proper reply to a notice or action by the United States Patent and Trademark Office. The date of abandonment is the day after the expiration date of the period set for reply in the Office notice or action plus an extensions of time actually obtained.

APPLICANT HEREBY PETITIONS FOR REVIVAL OF THIS APPLICATION

NOTE: A grantable petition requires the following items:
(1) Petition fee;
(2) Reply and/or issue fee;
(3) Terminal disclaimer with disclaimer fee --required for all utility and plant applications filed before June 8, 1995; and for all design applications; and
(4) Statement that the entire delay was unintentional.

1. Petition fee

☐ Small entity-fee $_____ (37 CFR 1.17(m)). Applicant claims small entity status. See 37 CFR 1.27.

☑ Other than small entity - fee $ 1,330.00 (37 CFR 1.17(m))

2. Reply and/or fee

A. The reply and/or fee to the above-noted Office action in the form of Reply under 37 CFR 1.111 and 3 month EOT (identify type of reply):
☑ has been filed previously on 3/22/2004 and 5/26/2004.
☐ is enclosed herewith.

B. The issue fee of $_____.
☐ has been paid previously on _____.
☐ is enclosed herewith.

06/29/2004 AWONDAF1 00000121 503120 10040077
01 FC:1453 1330.00 DA

3. Terminal disclaimer with disclaimer fee

☑ Since this utility/plant application was filed on or after June 8, 1995, no terminal disclaimer is required.

☐ A terminal disclaimer (and disclaimer fee (37 CFR 1.20(d)) of $_____ for a small entity or $_____ for other than a small entity) disclaiming the required period of time is enclosed herewith (see PTO/SB/63).

4. STATEMENT: The entire delay in filing the required reply from the due date for the required reply until the filing of a grantable petition under 37 CFR 1.137(b) was unintentional. [NOTE. The United States Patent and Trademark Office may require additional information if there is a question as to whether either the abandonment or the delay in filing a petition under 37 CFR 1.137(b) was unintentional (MPEP 711.03(c), subsections (III)(C) and (D))].

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June 25, 2004
Date


Signature

Telephone Number: 202-478-5300

Todd B. Buck, Reg. No.48,574
Typed or printed name

2121 K Street, NW,Suite 800
Address

Washington DC 20037
Address

Enclosures:
☑ Fee Payment
☐ Reply
☐ Terminal Disclaimer Form
☑ Additional sheets containing statements establishing unintentional delay
☐ Other: Courtesy Copy of Reply Filed 3/22/04 and 5/26/04

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being:

☐ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: **Mail Stop Petition**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

☐ transmitted by facsimile on the date shown below to the United States Patent and Trademark Office at (703) 872-9306.

Date

Signature

Type or printed name of person signing certificate

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
AMISS *et al.*	Art Unit: 1743
Appl. No. 10/040,077	Examiner: Alexander
Filed: January 4, 2002	Atty. Docket: 0709.017.0002
For: **Binding Proteins as Biosensors**	

Statement Under 37 C.F.R. §1.137(b)(3) that the Entire Delay in Filing the Required Reply was Unintentional

Assistant Commissioner for Patents
Mail Stop: Petitions
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Although neither Applicants nor their representatives have received a Notice of Abandonment in the above-captioned application, it is possible that the Office may have deemed this application abandoned for failure to reply within the statutory time period for reply, under 37 C.F.R. §1.135.

A non-final office action in connection with this application was mailed to Applicants representative on September 25, 2003. In response, Applicants timely filed a Reply under 37 C.F.R. §1.111 and a 3-month extension of time on March 22, 2004. Applicants' representative spoke with the Examiner on May 26, 2004, and learned that the Office had no record of receiving the March 22nd Reply. Applicants' representative immediately transmitted a copy of the March 22nd Reply, *via* facsimile, to the Examiner on May 26, 2004. The undersigned telephoned the Office on June 22, 2004 and spoke with the Office of Petitions, who indicated that the Office was in receipt of the May 26th facsimile, and that the 3-month extension of time had been granted. A courtesy copy of the March 22nd reply is enclosed herewith. As noted above, however, the Applicants have yet to be notified that the application has been abandoned for failure to reply in a timely manner.

Any period of abandonment of the above-captioned application that may be applicable was clearly unintentional. Indeed, the Applicants' March 22nd Reply and 3-month extension of time was a timely response to the Office Action of September 25, 2003. Additionally, Applicants' representative followed up with the Examiner after learning that the March 22nd Reply was apparently not received. Thus, neither Applicants nor their representative had any intention of abandoning this application. Accordingly, any "delay" in filing the required response from the Statutory deadline (March 25, 2004) to either May 26, 2004 or the date of this Petition was entirely unintentional.

Applicants respectfully petition the Assistant Commissioner to enter in the March 22nd Reply (of which the Office is in receipt as of May 26, 2004) and revive the above-captioned application, if it has been deemed abandoned.

It is not believed that any extensions of time or fees for net addition of claims are necessary beyond those that may be provided for in documents that may be accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required, including fees for net addition of claims, are hereby authorized to be charged to account number 50-3120.

Respectfully submitted,
CASTELLANO MALM FERRARIO & BUCK P.L.L.C.

Todd B. Buck, Ph.D.
Attorney for Applicants
Registration No. 48,574

Date: June 25, 2004
2121 K Street, NW.
Suite 800
Washington, D.C. 20037
(202) 478-5300

The Return of this post card, Properly stamped, will acknowledge receipt in the Patent & Trademark Office of the following:

1.- Petition For Extension of Time Under 37 CFR 1.136(a)
2.- Amendment and Response After Non-Final Rejection
3.-
4.-
5.-

Docket No.: P-5430 Serial No.: 10 /040,077

Filing Date: January 4, 2002 Date Mailed: March 22, 2004

Applicant(s) Amiss, Terry J. et al. Atty: JDW

Title: Binding Protein As Biosensors

Fee: $950.00 Charged to Deposit Account 02-1666

PTO/SB/22 (10-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional): P-5430

In re Application of: AMISS, TERRY J., et al.

Application Number: 10/040,077 — Filed: 01/04/02

For: BINDING PROTEIN AS BIOSENSORS

Group Art Unit: 1743 — Examiner: ALEXANDER, LYLE

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- ☐ One month (37 CFR 1.17(a)(1)) $_____
- ☐ Two months (37 CFR 1.17(a)(2)) $_____
- ☑ Three months (37 CFR 1.17(a)(3)) $ 950.00
- ☐ Four months (37 CFR 1.17(a)(4)) $_____
- ☐ Five months (37 CFR 1.17(a)(5)) $_____

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $_____.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account.

☑ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 02-1666.
I have enclosed a duplicate copy of this sheet.

I am the ☐ applicant/inventor

- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).
- ☐ attorney or agent of record.
- ☑ attorney or agent under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a): 42,207

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

March 22, 2004
Date

Jaconda Wagner
Signature

Jaconda Wagner, Esq.
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☑ Total of 2 forms are submitted.

PATENT
P-5430

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Amiss, Terry J., et al.

Title: BINDING PROTEIN AS BIOSENSORS

Application. No.: 10/040,077

Confirmation No.: 9417

Filing Date: January 4, 2002

Examiner: ALEXANDER, LYLE

Art Unit: 1743

AMENDMENT AND RESPONSE AFTER NON-FINAL REJECTION

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Arlington, VA 22313-1450

Sir:

In reply to the Examiner's Office Action dated September 25, 2003, the response having been extended by three (3) months to March 25, 2004, the following amendments and remarks are respectfully submitted in connection with the above-identified application.

Claim Amendments begin on page 2.

Remarks begin on page #10.

CLAIM AMENDMENTS

1. (Original) A glucose biosensor for in vivo or in vitro use comprising:
a) at least one mutated binding protein and at least one reporter group attached thereto such that said reporter group provides a detectable and reversible signal change when said mutated binding protein is exposed to varying glucose concentrations;
wherein said detectable and reversible signal change is related to said varying concentrations.

2. (Original) The biosensor of claim 1 wherein said mutated binding protein is glucose/galactose binding protein.

3. (Original) The biosensor of claim 1 wherein said binding protein has one amino acid substitution.

4. (Original) The biosensor of claim 1 wherein said binding protein has at least two amino acid substitutions.

5. (Original) The biosensor of claim 1 wherein said binding protein has at least three amino acid substitutions.

6. (Original) The biosensor of claim 3 wherein said one amino acid substitution is selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, and a cysteine at position 292.

7. (Original) The biosensor of claim 6 wherein said binding protein has at least one histidine tag.

8. (Original) The biosensor of claim 4 wherein said at least two amino acid substitutions are selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at

position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213.

9. (Original) The biosensor of claim 8 wherein said binding protein has at least one histidine tag.

10. (Original) The biosensor of claim 5 wherein said at least three amino acid substitutions are selected from the group consisting of a cysteine at position 149 and a serine at position 213 and a serine at position 238, and a cysteine at position 149 and an arginine at position 213 and a serine at position 238.

11. (Original) The biosensor of claim 10 wherein said binding protein has at least one histidine tag.

12. (Original) The biosensor of claim 1 wherein said reporter group is a luminescent label.

13. (Original) The biosensor of claim 12 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

14. (Original) The biosensor of claim 12 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

15. (Original) The biosensor of claim 12 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein.

16. (Currently Amended) The biosensor of claim 15 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), ~~Quantum Red®~~, (9-(2(or4)-(N-(2-maleimdylethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium salt) ~~(Texas Red®)~~, 2-(5-(1-(6-(N-(2-maleimdylethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-

propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt ~~(Cy3)~~, N-((2-iodoacetoxy)ethyl)-N-methyl)am- ino-7-nitrobenzoxadiazole ~~(IANBD)~~, 6-acryloyl-2-dimethylaminonaphthalene ~~(acrylodan)~~, pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt ~~(Lucifer Yellow)~~, 2-(5-(1-(6-(N-(2-maleimdylethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt ~~(Cy5)~~, ~~Dapoxyl~~™ 4-(5-(4-dimethylaminophenyl)oxazole-2-yl)-N- (2-bromoacetamidoethyl)sulfonamide, (N-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-s-indacene-2-yl)iodoacetamide ~~(Bodipy507/545 IA)~~, N-(4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-s-indacene-3-propionyl)-N- '-iodoacetylethylenediamine ~~(BODIPY™ 530/550 IA)~~, 5-((((2-iodoacetyl)amino)ethyl) amino)naphthalene-1-sulfonic acid ~~(1,5-IAEDANS)~~, and carboxy-X-rhodamine, 5/6-iodoacetamide ~~(XRIA 5,6)~~.

17. (Withdrawn) A method for glucose detection comprising:

(b) providing at least one mutated glucose/galactose binding protein and at least one reporter group attached thereto;

(c) exposing said mutated glucose/galactose binding protein to varying glucose concentrations;

(d) detecting a detectable and reversible signal change from said reporter group wherein said detectable and reversible signal change corresponds to said varying glucose concentrations.

18. (Withdrawn) The method of claim 17 wherein said detecting is continuous, programmed, episodic, or combinations thereof.

19. (Withdrawn) The method of claim 17 wherein said mutated glucose/galactose binding protein is selected from bacterial periplasmic binding proteins.

20. (Withdrawn) The method of claim 17 wherein said detecting of detectable and reversible signal changes from said reporter group of varying glucose concentrations is in vivo.

21. (Withdrawn) The method of claim 17 wherein said binding protein has one amino acid substitution.

22. (Withdrawn) The method of claim 17 wherein said binding protein has at least two amino acid substitutions.

23. (Withdrawn) The method of claim 17 wherein said binding protein has at least three amino acid substitutions.

24. (Withdrawn) The method of claim 21 wherein said one amino acid substitution is selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, and a cysteine at position 292.

25. (Withdrawn) The method of claim 24 wherein said glucose/galactose binding protein has at least one histidine tag.

26. (Withdrawn) The method of claim 22 wherein said glucose/galactose binding protein has at least two amino acid substitutions selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213.

27. (Withdrawn) The method of claim 26 wherein said glucose/galactose binding protein has at least one histidine tag.

28. (Withdrawn) The method of claim 23 wherein said glucose/galactose binding protein has at least three amino acid substitutions selected from the group consisting of a cysteine at

position 149 and a serine at position 213 and a serine at position 238, and a cysteine at position 149 and an arginine at position 213 and a serine at position 238.

29. (Withdrawn) The method of claim 28 wherein said glucose/galactose binding protein has at least one histidine tag.

30. (Withdrawn) The method of claim 17 wherein said at least one reporter group is a liminescent label.

31. (Withdrawn) The method of claim 30 wherein said luminescent label has an excitation wavelenth of more than about 600 nanometers.

32. (Withdrawn) The method of claim 30 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

33. (Withdrawn) The method of claim 30 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with said at least one mutated binding protein and a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), Quantum Red™, Texas Red™, Cy3, N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan),pyrene, Lucifer Yellow,Cy5, Dapoxyl® (2-bromoacetamidoethyl)sulfonamide, (*N*-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-*s*-indacene- 2-yl)iodoacetamide (Bodipy507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-*s*-idacene- 3-propionyl)-*N'*-iodoacetylethylenediamine (BODIPY® 530/550 IA), 5-((((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

34. (Withdrawn) A composition comprising:

a mutated glucose/galactose binding protein having at least one amino acid substitution selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position

107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, and a cysteine at position 292.

35. (Withdrawn) The composition of claim 34 wherein said mutated glucose/galactose binding protein has at least one histidine tag.

36. (Withdrawn) The composition of claim 34 wherein said mutated glucose/galactose binding protein further has at least one reporter group.

37. (Withdrawn) The composition of claim 36 wherein at least one reporter group is a luminescent label.

38. (Withdrawn) The composition of claim 37 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

39. (Withdrawn) The composition of claim 37 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

40. (Withdrawn) The composition of claim 37 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with said at least one mutated binding protein and a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), Quantum Red™, Texas Red™, Cy3, N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan),pyrene, Lucifer Yellow,Cy5, Dapoxyl® (2-bromoacetamidoethyl)sulfonamide, (*N*-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-*s*-indacene- 2-yl)iodoacetamide (Bodipy507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-*s*-idacene- 3-propionyl)-*N'*-iodoacetylethylenediamine (BODIPY® 530/550 IA), 5-((((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

41. (Withdrawn) A composition comprising:

a mutated glucose/galactose binding protein having at least two amino acid substitutions selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an argine at position 213, and a cysteine at position 149 and a serine at position2 13 and a serine at position 238, and a cysteine at position 149 and an arginine at poistion 213 and a serine at position 238.

42. (Withdrawn) The composition of claim 41 wherein said mutated glucose/galactose binding protein has at least one histidine tag.

43. (Withdrawn) The composition of claim 41 wherein said mutated glucose/galactose binding protein further has at least one reporter group.

44. (Withdrawn) The composition of claim 43 wherein at least one reporter group is a luminescent label.

45. (Withdrawn) The composition of claim 44 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

46. (Withdrawn) The composition of claim 44 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

47. (Withdrawn) The composition of claim 44 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with said at least one mutated binding protein and a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA Quantum Red™, Texas Red™, Cy3, N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan),pyrene, Lucifer Yellow, Cy5, Dapoxyl® (2-bromoacetamidoethyl)sulfonamide, (*N*-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-*s*-

indacene- 2-yl)iodoacetamide (Bodipy507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-*s*-idacene- 3-propionyl)-*N'*-iodoacetylethylenediamine (BODIPY® 530/550 IA), 5-((((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

REMARKS

Claims 1-16 are pending in the application. Claims 17-47 were withdrawn pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention. The election was made without traverse in Paper No. 11. Claim 16 has been amended to recite the generic name for the dyes instead of using the trademark name. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the remarks that follow.

REJECTIONS

Rejection of Claim 16 under 35 USC §112, second paragraph.

The Examiner has rejected claim 16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner asserts Applicants are claiming trademarked labels for which Applicant must claim the compound and not the trademarked compound. Applicants have amended claim 16 to recite the known chemical name of the previously recited trademarks at the time the invention was filed. No new matter is believed to be introduced by this amendment.

Quantum Red™ has been deleted. Texas Red maleimide is disclosed in TABLE 1, and the term Texas Red ™ is replaced by its known IUPAC name--(9-(2(or4)-(N-(2-maleimdylethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium, inner salt). Lucifer Yellow IA is disclosed in TABLE 1, and the term Lucifer Yellow is replaced by its known IUPAC name--6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt. Cy3 and Cy5 have been replaced by their IUPAC names, 2-(5-(1-(6-(N-(2-maleimdylethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt, and 2-(5-(1-(6-(N-(2-maleimdylethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt, respectfully. Dapoxyl® radical has been replaced by its IUPAC name--4-(5-(4-dimethylaminophenyl)oxazole-2-yl)-N (2-bromoacetamidoethyl)sulfonamide. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections of Claims 1-16 for Double Patenting

The Examiner has provisionally rejected Claims 1-16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 and 1-12 of co-pending Application No. 10/039,833 and 10/039,799 respectively. The Examiner asserts that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because both are directed to a biosensor using the same mutated binding protein." Applicants respectfully traverse the rejection.

The subject matter recited in the claims of the instant case is related to biosensors having mutated binding protein and reporter group attached thereto, such that the reporter group provides a detectable and reversible signal change when the mutated binding protein is exposed to varying glucose concentrations, and wherein the detectable and reversible signal change is related to the varying concentrations.

Claims 1-22 of co-pending Application No. 10/039,833 recite elements not recited in the instant claims. Specifically, claims 1-22 of co-pending Application No. 10/039,833 recite a biosensor having mutated binding protein and reporter group attached thereto, and b) an analyte permeable matrix entrapping or encapsulating the mutated binding protein. The instant claims are patentably distinct from co-pending Application No. 10/039,833.

Claims 1-12 of co-pending Application No. 10/039,799 recite elements not recited in the instant claims. Specifically, claims 1-12 of co-pending Application No. 10/039,799 recite a biosensor having mutated binding protein and reporter group attached thereto, *and at least one sensor surface wherein the mutated binding protein is thiol-coupled.* The instant claims are patentably distinct from co-pending Application 2003/0134346.

Reconsideration and withdrawal of the double patenting rejection is requested.

Rejection of Claims 1-5 under 35 USC § 102(e) as being anticipatedby Kratzch et al.

The Examiner has rejected Claims 1-5 under 35 U.S.C. 102(e) as being anticipated by US application 2003/0104595 by Kratzch et al., (Kratzch '595). The Examiner states, "Kratzch et al. teach in paragraph [0008] that glucose biosensors using s-GDH(glucose dehydrogenase) are well known in the art. In paragraphs [0002] + teach the instant invention is to creating an improved s-GDH variant by mutating the binding protein." Applicants respectfully traverse the rejection.

As the Federal Circuit has held, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). *See* MPEP § 2131.

Kratzch '595 fails to teach every element of the claim. Specifcially, Kratzch '595 fails to teach or suggest a reporter group attached to the protein. Kratzch '595 teaches pyrrolpquinoline (PQQ)-dependent, mutant-GDH's. PPQ is a non-covalently bound quinone acting as a co-factor to GDH, which by way of reduction, constitutes the reporter group. (See Example 2, paragraphs

[0102] thru [0112], disclosing the addition of PPQ to agar plates of mutant GDH's). In contrast, Applicants claims 1-5 are explicit in their requirement that reporter group be attached to the binding protein. Accordingly, the claims of the current application are not anticipated by Kratzch '595. Reconsideration and withdrawal of the Examiner's Rejection is respectfully requested.

Rejection of Claims 1-5 under 35 U.S.C. 102 (e) as being anticipated by 6,277,627 to Hellinga, 6,521,446 to Hellinga, and 6,197,534 to Lakowicz

The Examiner has rejected Claims 1-5 under 35 U.S.C. 102(e) as being anticipated by 6,277,627 to Hellinga (Hellinga '627), 6,521,446 to Hellinga (Hellinga '446) and 6,197,534 to Lakowicz et al. (Lakowicz '534). The Examiner states, "[t]hese references all teach use of a mutated protein in combination with a glucose biosensor." Applicants respectfully traverse the rejection.

As discussed above, to anticipate a claim, each and every element of the claimed invention must be taught by the prior art. The cited references, Hellinga '627, Hellinga '446 or Lakowicz '534 fail to teach all of the elements of the claim. Specifically, the references fail to teach that at least one reporter group attached to the protein provides a reversible signal change when the mutated binding protein is exposed to *varying* glucose concentrations. Accordingly, the pending claims of the current application are not anticipated by Hellinga '627 , Hellinga '446 or Lakowicz et al. references. Reconsideration and withdrawal of the Examiner's Rejection is respectfully requested.

Rejection of Claims 1-5 and 11-16 under 35 U.S.C. 102(e) as being anticipated by Marvin et al., Marvin et al., or Tolosa et al.

The Examiner has rejected Claims 1-5 and 11-16 under 35 U.S.C. 102(e) as being anticipated by Marvin et al., *J. Am. Chem. Soc.* (1998) 120:7-11, Marvin et al., *Proc. Natl. Acad. Sci.* (1997) 94:4366-4371, or Tolosa et al., *Anal. Biochem.* (1999) 267:114-120. The Examiner states, "[t]hese references all teach glucose biosensors using a mutated binding protein to quantify glucose using fluorescent measurements." Applicants respectfully traverse the rejection.

Marvin et al. (*J. Am. Chem. Soc.* 1998) teaches single site mutated glucose binding proteins (GGBP) incorporating allosterically and non-allosterically linked fluorescent groups.

Marvin et al. fails to teach a reversable signal change from the reporter group when exposed to varying glucose concentrations. The reference fails to teach all the elements of Applicant's claim.

Marvin et al. (*Proc. Natl. Acad. Sci.* 1997) teaches mutation of maltose binding protein (MBP). Marvin et al. expressly states on page 4369 (last incomplete sentence, continuing on p. 4370), "[t]he mutants do not respond to glucose...and are therefore still specific for maltose." The reference fails to teach all the elements of Applicant's claim.

Tolosa et al., *Anal. Biochem.* (1999) 267:114-120 teach single site mutant GGBP and phase modulated fluorimetry for glucose detection. The reference fails to teach a reversible signal change from the reporter group when exposed to varying glucose concentrations. The reference teaches only titration of protein with glucose (p. 117). The reference fails to teach all the elements of Applicant's claim.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection of Claims 6-10 under 35 U.S.C. 103(a) as being unpatentable over Marvin et al., *J. Am. Chem. Soc.* (1998) 120:7-11, Marvin et al., *Proc. Natl. Acad. Sci.* (1997) 94:4366-4371, or Tolosa et al., *Anal. Biochem.* (1999) 267:114-120

The Examiner has rejected Claims 6-10 under 35 U.S.C. 103(a) as being unpatentable over Marvin et al., *J. Am. Chem. Soc.* (1998) 120:7-11, Marvin et al., *Proc. Natl. Acad. Sci.* (1997) 94:4366-4371 or Tolosa et al., *Anal. Biochem.* (1999) 267:114-120, stating, "[t]hese references all teach glucose biosensors using a mutated binding protein to quantify glucose using fluorescent measurements." The Examiner also relies on *In re Boesch*, and states [i]t would have been within the skill of the art to modify Marvin et al., (J AM Chem. Soc. 1998,120,7 cite by Applicants), Marvin et al. (Proc. Natl. Acad. Sci. cited by Applicant) or Tolosa et al. (Analytical Biochemistry 267,114-120 (1999) cited by Applicants) and modify the amino acids at the claimed positions as optimization of a result effective variable." Applicants respectfully traverse the rejection.

Optimization of a result-effective variable is based on the assumption that the result-effective variable is predictable and already known. Choosing amino acids to modify and the specific mutation positions as being a result effective variable is not predictable or known to provide a particular result. The Circuit Court for Patent Appeals has stated that, while it may

ordinarily be the case that the determination of optimum values for the parameters of a prior art process would be at least prima facie obvious, that conclusion depends upon what the prior art discloses with respect to those parameters. *See In re Sebek*, 465 F.2d 904 (C.C.P.A. 1972). In the teachings of the references it is expressly recited that choice of specific mutation position (or which amino acids) to modify was not reasonably predictable and was not known and thus cannot be previously recognized as result-effective. (For example, see Marvin et al. *J. Am. Chem. Soc* 1988, p. 9, stating: "[s]ince it is impossible to predict which of the residues in the flap region is likely to give the most pronounced allosteric response to ligand binding, we choose to scan the b-sheet portion of the flap and identified four sites for reporter group attachment.") Thus, the choice of amino acid and mutation position as a result effective variable is not one that is predictable and provides well-known results. It follows therefore, the choice of amino acids and mutation positions cannot be relied upon to 'optimize'.

Applicants respectfully request withdrawal and reconsideration of the rejection.

Rejection of Claims 6-16 under 35 U.S.C. 103(a) as being unpatentable over Hellinga (6,277,627), Hellinga (6,521,446) or Lakowicz et al.

The Examiner has rejected Claims 6-16 under 35 U.S.C. 103(a) as being unpatentable over Hellinga '627, Hellinga '446 or Lakowicz '534 stating, "[i]t would have been within the skill of the art to modify Hellinga (6,277,627), Hellinga (6,521,446) or Lakowicz et al. and modify the claimed amino acids at the claimed positions as optimization of a result effective variable." The Examiner also states, "[i]t would have been within the skill of the art to further modify Hellinga (6,277,627), Hellinga (6,521,446) or Lakowicz et al. and use well known fluorescent labels, such as Quantum Red™, Texas Red™, etc., to gain the above advantages and as optimization of a result effective variable." Applicants respectfully traverse the rejection.

As discussed above, the choice of amino acid and mutation positions as a result effective variable is not one that is predictable with well-known results. Likewise, the environment of any attached reporter group in the analyte-bound and analyte-unbound configurations of the protein is not reasonably known and cannot be predicted. The reporter group, either alone or in combination with the specific amino acid substitution and mutation position cannot be a result-effective variable. Further, Applicant's choice of amino acid substitutions and reporter group combination provides for more than four fold enhancement of signal (see Table 2). That any

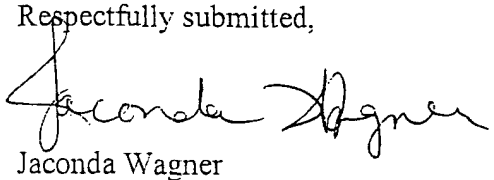
combination of amino acid substitutions in combination with any reporter group would provide substantially improved signal over a single or multiple mutation of the protein and reporter group is an unexpected result. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

Favorable reconsideration of the claims as amended and the remarks presented herein is respectfully requested. Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Jaconda Wagner (Reg. No. 42,207) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-1666 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,



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